REMARKS

This application pertains to novel solid lipid particles of bioactive agents and methods for the manufacture and use thereof.

Claims 1-45 are pending.

Claims 1-15 and 37-39 are withdrawn from consideration, while Applicant still desires to traverse the restriction requirement.

Reconsideration and withdrawal of the restriction requirement is respectfully requested as for the reasons already stated in the response to the restriction requirement.

In case the Examiner still does not find it possible to withdraw the restriction requirement, it is respectfully requested that the non-elected subject matter be rejoined with the elected subject matter upon allowance of the elected subject matter.

Amendments to Claims

The amendments made herein are necessary to obviate the concern raised by the Examiner that no specific sequence is mentioned for steps a, b, c, d and e. Although Applicants believe that those skilled in the art would have understood that each of the steps are performed in order, i.e, b) after a), c) after b), d) after c) and e) after d), the Examiner has raised the issue and Applicants are amending the claims to obviate the Examiner's concerns. Certain other amendments are being made at the same time to improve the from of the claims, especially with respect to antecedent support issues.

Claim 42 has been amended to correct the spelling error "C" to "C)" to refer to the additives C). Support is found in para. [0057] of the disclosure of the description.

No new matter is introduced.

Rejections under 35 USC § 103

Claims 16-36 and 40-45 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Westesen et al. (US 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 2000, 16, 402-407).

Applicants again refer to the arguments made in response to the first office action wherein it was noted that the process according Westesen et al. does not only fail to disclose addition of compressible fluid in the supercritical state to the suspension, but additionally fails to disclose the property of suspending at least one active substance A), which is solid at room temperature (...) in an aqueous phase.

As previously pointed out Westesen et al. discloses a method to form solid lipid particles (SLP's) by melting solid lipids (col. 11, line 6) and dispersing the melt into the dispersion medium to form an emulsion (col 11, lines 25-30), while the melt may contain bioactive agents in molten, dissolved, solubilized or dispersed form (col. 11, lines 16-20).

Additionally it is disclosed by the Westesen et al. reference, that the "matrix of the SLPs is constituted by (...) hydrophobic materials" (col. 9, lines 20-22) and that "poorly water-soluble" drugs are preferred (col. 10, lines 20-22). Furthermore, if these drugs are not poorly water-soluble "it is necessary to decrease the water-solubility of this component" (col. 10, lines 26-30).

The active substance is always incorporated into the lipid melt, prior to contacting said mixture with the dispersion medium. Said contacting may be melting together with the lipid or dissolution, solution or dispersion in a lipid-melt (see col. 11, lines 16-20). It is most likely that dissolution or solution is desired due to the correspondent hydrophobic properties of the lipids and the active substances, but in none of these possibilities is the active substance suspended in an aqueous phase

Therefore the limitation of Applicants Claims 16, 26 and 40, wherein "active substance A) (...) is suspended in an aqueous phase" is not met.

Furthermore Westesen et al. discloses melting meltable bioactive agents and forming dispersions of such by a process similar to the forming SLP's (col. 14, lines 19-26). Hence the bioactive agents are not suspended in an aqueous phase, but melted and emulsified in a heated dispersing medium.

Accordingly the invention according to the disclosure of Westesen et al. pertains to a method of melting and emulsification in a pre-heated dispersion medium as an inevitable step to come to work.

The Examiner contends that the aforesaid argumentation is not persuasive, as "the claims recite the process comprising: a, b, c, d and e, however no specific sequence is mentioned." It is further stated by the Examiner that "the prior art, when taken as a whole, teaches all the steps, however in a different sequence."

Applicants have now amended their claims to clarify that the steps are in sequence. Thus, for example, step b) refers to the suspension formed in a), step c) refers to the mixture

formed in b) step d) refers to the dispersion formed in c) and step e) refers to the homoginzied dispersion, which clearly is formed in the immediately preceeding step d),

Claims 16, 26 and 40 clearly reflect sequences of steps.

It should be clear to someone of ordinary skilled in the art to start a process with step a). In all of the Claims 16, 26 and 40 step b) is thereafter performed with the "suspension formed in a)". Furthermore step c) is always performed with "the mixture formed in b)". Thereafter the " dispersion formed in c)" is further handled in step d). From this reading it is absolutely clear to someone of ordinary skill in the art that the final step e) can only be performed after step d), as said step e) always refers to a further handling of "the homogenized dispersion", which was formed in c) and homogenized in d) as outlined before. Therefore no other meaning is possible.

This particular sequence ensures the desired and already in reply to the previous office action described minimization of an emulsified state of the system to a maximum of a few milliseconds (see paragraph [0132], last sentence) further using a process defined by the existence of suspended particles even before passing the short emulsion step.

Therefore, as the examiner has already pointed out correctly, neither the particular sequence and hence nor the "suspending at least one active substance A), which is solid at room temperature (...) in an aqueous phase" is disclosed in the Westesen et al. reference.

The disclosure of Timothy et al. does not help to overcome these general discrepancies between Westesen et al. and Applicant's inventive process disclosed in Claims 16-36 and 40-45.

From the foregoing, it is clear that Applicants' claims are not unpatentable over Westesen et al. (US 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 2000, 16, 402-407) and the rejection of claims 16-36 and 40-45 under 35 U.S.C. 103(a) as obvious over Westesen et al. (US 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 2000, 16, 402-407) should now be withdrawn.

In view of the present amendments and remarks it is believed that claims 16-36 and 40-45 are now in condition for allowance. Reconsideration of said claims by the Examiner is respectfully requested and the allowance thereof is courteously solicited.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Applicant requests that this be considered a petition therefor. Please charge the required petition fee to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fee or credit any excess to Deposit Account No. 14-1263.

Respectfully submitted,
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